Validation of two-dimensional speckle tracking strain for assessment of early right ventricular dysfunction: in vivo and ex vivo study


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**Background** Right ventricular (RV) dysfunction is a major determinant of long-term survival in congenital heart diseases. Early echo detection of RV failure is mandatory, but recent indices need to be validated.

**Aims** Objectives were to: (1) validate standard and strain echo indices for evaluation of RV systolic function, compared to hemodynamic parameters; (2) assess the accuracy of these indices for early detection of RV failure.

**Methods** Combined RV overload as observed in repaired tetralogy of Fallot was surgically reproduced in 2-month-old pigs (n=6). Age-matched piglets were used as controls (n=4). RV function was evaluated at baseline and 4 months of follow-up by standard and strain echo indices, compared to conductance catheter. Sarcomere shortening and calcium transients were recorded in RV isolated myocytes (IonOptix). Contractile reserve was assessed by in-vivo (dobutamine 5μg/kg) and ex-vivo (isoprorenaline 100nM) β-adrenergic stimulation. The integrity of T-tubules was controlled after Di-4-Anepps labeling.

**Results** 4 months after surgery, hemodynamic RV ejection fraction (FEVD) was significantly decreased (29.7% [26.2-34] vs 42.9% [40.7-48.6], p<0.01), and inotropic responses to dobutamine were blunted (contractile reserve ΔEmax=51% vs 193%, p<0.05). On echocardiography FAC, TAPSE, S’ peak and RV free wall longitudinal rate were significantly reduced and correlated with FEVD. Peaks strain rate and S’ were correlated with ΔEmax (r=0.75 vs 0.78, p<0.05). Isolated RV myocytes from operated animals showed hypertrophy, decreased sarcomere shortening peak in response to isoprorenaline (ΔL=7.8±2.8% vs 10.7±2.9%, p<0.05), and increased spontaneous calcium waves suggesting perturbations of calcium homeostasis.

**Conclusion** In this model, both standard and strain echo indices allowed the detection of early impairments of RV function and cardiac reserve, which are associated with cardiac excitation-contraction coupling alterations.

The author hereby declares no conflict of interest

0292

Cardiac phenotype and prognosis of patients with mutations in Nkx2.5 gene

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**Introduction** Mutations in Nkx2.5 gene explain familial forms of atrial septal defect (ASD) associated with atrioventricular conduction disturbances and unexplained sudden death (SD) but cardiac phenotype has not been described in a large population of patients with Nkx2.5 mutations.

**Methods** all successive patients with mutations in Nkx2.5 gene were included, representing the whole population of French Nkx2.5 mutated patients.

**Results** 47 pts carried Nkx2.5 gene mutations (24 men, median 25 yo, 0 to 69) (20 unrelated families, 2.5±1.5 mutated subject/family). There was an history of SD in 9 and of pace-maker implantation in 5 families. ASD was present in 70% (surgically corrected in 67% and percutaneously in 2 pts) and ventricular septal defect in 15%. Conduction disturbances were observed in 82%, 13 pts (27%) developed complete or high degree AV block. Available ECGs showed PR interval of 219±43 ms, QRS duration of 86±15ms and a QTc of 408±27ms. Electrophysiological study was performed in 15 pts (3 had infra hisian and 5 supraventricular block). A pace-maker was implanted in 20 pts (with ICD in 5) and a loop recorder in one. Sustained or nonsustained ventricular tachycardia were observed in 6 pts. Mean ventricular pacing % was 77±37. Six pts were dependent of the pace-maker. Three patients deceased over the follow-up (2 SD and one endocarditis), 13 pts developed paroxysmal or permanent supraventricular arrhythmias (mainly atrial fibrillation). Five pts displayed dilated cardiomopathy, 3 had left ventricular (LV) hypertrophy and 4 with features of noncompacted LV. LV ejection fraction was normal except in 2 cases (35%).

**Conclusion** carriers of Nkx2.5 gene mutations harbor a rich phenotype associated most of the time ASD and/or SD together with evolutive AV block leading to pace-maker/ICD implantation in a significant part of them. Associated LV cardiomopathy is less frequent but ventricular arrhythmias appear common and SD may happen.

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